REMARKS

1. The present application as originally filed contained claims 1-26. Claims 16–18 have been amended. Support for the amendments can be found throughout the application. Specifically, support for the amendment reciting the term "substrate" can be found in the specification, for example, at page 5, line 27 through page 6, line 15, which describes that isolation of antigen-specific T cells utilizes MHC-coated substrates. Accordingly, the amendments do not constitute new matter and entry thereof is respectfully requested. Applicants have carefully reviewed the rejections set forth in the Office Action and respectfully traverse all grounds for the reasoning which follow.

2. Regarding Priority to provisional application 60/025,558, the specification states, at page 5, lines 31–32, that a wide variety of substrates are suitable for use in the present invention. One of ordinary skill in the art would readily be able to purchase substitute products and readily incorporate them into the present invention. It is therefore believed that the present application is fully entitled to the priority date of the provisional application.

REJECTIONS UNDER 35 U.S.C. § 112

1. Claims 16 – 18 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, claim 16 stands rejected for recitation of the word "matrix" allegedly because it is unclear what is encompassed by this term. Claim 16 was also rejected for the recitation "Class I peptide" because the Examiner alleges such recitation is indefinite and ambiguous. Claim 17 stands rejected for recitation of the word "bead" allegedly because this term is not defined in the specification.

2. Applicants contend that the objected terms are sufficiently clear to those skilled in the art to allow the invention to be practiced as claimed. Nevertheless, to further prosecution of the application, claim 16 has been amended to recite "Class I molecules", and to recite that the support, having on its surface an immobilized empty MCH Class I molecule, is a substrate. Therefore, this amendment renders rejections of claim 16 moot and its withdrawal is respectfully requested.

3. Regarding rejection of claim 17 over the use of the term "bead", Applicants contend that the term is sufficiently clear for those skilled in the art to practice the invention as claimed. The term "bead", as it is used in the biochemical sciences, is an art-recognized term for a substrate having particle properties. Moreover, the present specification describes beads as substrates, for example, at page 6, lines 4–5, and provides several different types of exemplary beads that can be used in the methods of the invention. For example, at page 6, lines 4–9, the specification describes that "a wide variety of MHC coated substrates are suitable for use in the present invention, including, but not limited to, ...glass beads, latex beads, ...and magnetic beads, with magnetic beads being preferred." Further, on page 6, lines 26–29, and throughout the Examples beginning on page 10, the specification additionally teaches the use of avidin-coated magnetic beads for use as a substrate for capturing antigens. Polystyrene latex sulfate beads are additionally described in the Examples at, for example, page 11, lines 10–12. Finally, for the commercially available beads used in the studies described in the Examples, the specification provides relevant information for the manufacturer. In light of the art-recognized meaning and the teachings in the specification, Applicants content that the meaning of the objected term is clear to those skilled in the art. Accordingly, this ground of rejection is respectfully requested to be withdrawn.

4. The Examiner also rejected claims 16–18 for the use of the term "peptide" with respect to the empty Class I complex. The term "molecules" has been inserted in place of "peptide" after Class I in claim 16. It is therefore believed that the claims as amended herein satisfy the requirements of 35 U.S.C. § 112, second paragraph.

REJECTIONS UNDER 35 U.S.C. §102 (e)

1. Claims 16–18 stand rejected under 35 U.S.C. §102 (e) as allegedly anticipated by U.S. Patent No. 5,731,160, to Melief et al. The Office Action states that U.S. Patent No. 5,731,160, describes antigen-presenting liquid bi-layer carrying vehicles, including liposomes, incorporating empty MHC molecules that are capable of binding peptide antigens. The Office Action concludes that lipid bi-layer carrying vehicles, or liposome, is encompassed by the terms "matrix" and "bead" as used in the claimed invention. The term "matrix" has been deleted from the present claims, and "substrate" has been inserted in its place in this amendment. The claims, as amended, are therefore directed to a substrate for capturing antigens comprising a support having an immobilized empty Class I peptide. Applicants contend that a substrate for capturing antigens is distinct from the lipid bilayer vehicle or liposome as described in U.S. Patent No. 5,731,160, (herein after referred to as Melief et al.)

2. Melief et al. describes the expression of empty MHC Class I molecules on cells that can be loaded with exogenous immunogenic peptides (see, for example, column 5, lines 48–51). The methods are extended by analogy to Melief et al. at column 5, lines 53–55, to all antigen-presenting lipid bi-layer carrying vehicles. There is no description in Melief et al. of using alternatives or substitutes other than lipid bi-layers to simulate the native conformation and functions found through expression of MHC Class I molecules. Therefore, and as set forth further below, expression of empty MHC Class I molecules in

cells, or incorporation into a lipid bi-layer as described by Melief et al., is distinct from the invention as described and claimed in the above-identified application.

3. As taught in the present specification, and as claimed in amended claim 16, a substrate for capturing antigen is a material distinct from a lipid bi-layer because it is a support that has on its surface an immobilized purified MHC Class I molecule. Therefore, the substrates of the claimed invention are coated, absorbed or attached with purified empty MHC Class I peptides. Melief et al. does not teach a purified MHC Class I molecule, but utilizes cell lines wherein the cells have, in their membranes, empty MHC Class I molecules.

4. The present specification teaches methods for immobilizing the MHC Class I peptides onto a substrate. None of such methods are directed to insertion into a lipid bi-layer through a transmembrane region of a MHC Class I receptor. Instead, the application teaches that those skilled in the art can practice the invention as claimed by, for example, coating, absorbing or attaching empty MHC Class I peptides to various substrates, such as those described above. For example, the specification teaches, at page 6, lines 9–15, a variety of methods suitable for immobilizing an empty MHC Class I peptide by, for example, passive absorption (page 6, line 11), cross-linkers (page 6, line 11), biotin-avidin affinity absorption (page 6, line 12), and other affinity interactions, including antibody affinity interactions (page 6, lines 12 – 15). Therefore, the claimed substrates are distinct from the lipid bi-layer carrying vehicles or liposomes of Melief et al. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

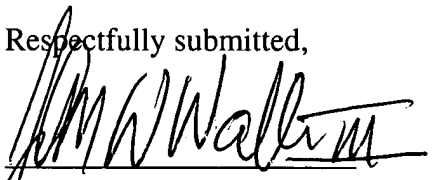
5. In addition, claim 16 has been amended to recite that the Class I MHC molecules were purified. Support for this amendment is found throughout the specification, in particular in Example 1. Melief et al. utilizes Class I molecules as produced in the cell lines without a purification step, as set forth in claim 16 as amended herein.

CONCLUSION

1. In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance, and respectfully request a notice to this effect.

2. No fee is believed to be due as a result of this amendment. Please charge any deficiency or credit any overpayment to Deposit Account No. 10-0750/ORT-1060/JWW. This form is submitted in triplicate.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Page 1, after **TITLE OF THE INVENTION**, PURIFICATION OF ANTIGEN-SPECIFIC T CELLS, please insert the following paragraph:

CROSS-REFERENCE TO RELATED APPLICATION

This application is a divisional application of U.S. Application No. 08/909,549, filed 12 August 1997, abandoned, which is based on, and claims the benefit of, U.S. Provisional Application No. 60/025,588, filed 6 September 1996.

In the Claims:

Claim 16 is amended as follows:

16. (Amended) A ~~matrix~~ substrate for capturing antigens, comprising a support having on its surface purified immobilized empty Class I molecules ~~peptide~~, wherein said Class I molecules are ~~peptide is~~ capable of binding one or more antigens.

Claim 17 is amended as follows:

17. (Amended) The ~~matrix~~ substrate of claim 16 wherein the matrix is a bead.

no ant basis

Claim 18 is amended as follows:

18. (Amended) The ~~matrix~~ substrate of claim 16 wherein the antigen is a peptide.

singular vs plural